

MIGRAINE AND ALLERGY¹

By

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During the past few decades, it has been asserted in a large number of investigations, particularly in the United States, that migraine should be regarded as an allergic disease (Vaughan, 1927; survey by Vaughan and Black, 1948). This view is based on the following observations: (1) occurrence of allergic manifestations in the migraine patients themselves, as well as in their relatives; (2) according to the sick history appearance of attacks after the ingestion of certain foods; (3) positive skin tests indicating specific hypersensitiveness; (4) positive results of exposure to specific allergens; (5) good therapeutic results with desensitization and/or elimination diet.

Since the autumn of 1947, we have been analysing the allergic picture in some of the approximately 250 cases of migraine we have had under observation in connection with studies of the migraine syndrome in different ages (Vahlquist et al., 1949).

Material: 40 cases of migraine have been examined, 25 of them women and 15 men. The youngest patient was five years old and the oldest 49. The age group, 5 to 14 years, comprised 15 patients. All the cases presented a typical picture of migraine. In addition to paroxysmal headache, they had at least two and often three or four of the following characteristics: typical heredity, nausea, flimmer scotoma and hemicrania. In selecting our material, we gave priority to patients who had relatively frequent and severe attacks,

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and we also favoured patients who lived near enough to the hospital to be able conveniently to report for examinations.

Method: A detailed history was taken down of all the cases, with special attention to allergic manifestations in the patients themselves and also in their parents and siblings. All the patients were submitted to skin testing by the intracutaneous method. Tests were made with forty of the nutrition and inhalation allergens commonly met with in Sweden.

The inhalation allergens included dust and pollen extracts, extracts of feathers, straw, hay, lycopod, mould, wool, cattle and horse, cat and dog hair. The nutritive allergens included chocolate, fish and meat of various kinds, lobster, yeast, cereals, milk, egg, and different kinds of vegetables. The reaction was read about twenty minutes after the injection of the allergen, and the positive results were evaluated in relation to the histamine weal used as a control.

Experiments with exposure were made in a few cases, in which the history or the skin test had given us reason to suspect the presence of allergy.

In 14 cases the patients were treated with Antasten,¹ an antihistamine preparation. Here priority was given to persons who had given positive reactions to the intradermal tests.

Results: In order to facilitate evaluation of the results, we have collected a material for comparison, which consists of a series of 40 asthmatic children treated at the Norrtull Hospital in the year 1947 and of a normal series comprising 80 adults, all of them employed at the hospital.

Allergic diseases in parents and siblings are presented in Table 1, from which it appears that the incidence of positive allergic heredity in the present material does not differ substantially from that in the normal material. There is an appreciable numerical difference in the incidence of eczema as compared with the asthma material. The total incidence of allergic manifestations is 14 per cent in the migraine group and 33 per cent in the asthmatic group. The difference, 19 ± 5.1 per cent, is statistically significant. However, it should be borne in mind that the data in the asthma group were provided by the mother and undoubtedly are more complete than in the migraine group, in which the

¹ We are indebted to AB *Ciba-Produktion* for their kindness in supplying us with *Antasten* (*Antistin*).

TABLE 1

The incidence of allergic diseases in close relatives of patients with migraine and asthma as compared with normal subjects.

	Total no. of parents and siblings	In parents and siblings				
		Asthma	Eczema	Urtica- ria	Hay- fever	Other allergy
Migraine material (38 cases)	156	4 %	4 %	5 %	0	1 %
Asthma material (40 cases)	117	6 %	13 %	6 %	6 %	2 %
Normal material (80 cases)	371	3 %	3 %	4 %	2 %	1 %

patients themselves usually supplied the information. In view of this, the differences are remarkably small between the migraine and the normal material on the one hand and the asthma material on the other.

With regard to the presence of allergic diseases in the patients themselves, the figures are about the same for the migraine and the normal material, as appears in Table 2. The asthmatic children show considerably higher rates for eczema, urticaria, and "other" allergic diseases. In this case, too, it must be assumed that the data for the asthmatic patients are more complete than for the other groups, since the mothers obviously had clearer memories of the illnesses of early childhood than the patients themselves.

The unreliability of second-hand information appears

TABLE 2

The incidence of allergic diseases in patients with migraine and asthma as compared with normal subjects.

	Number exami- ned	Asthma	Eczema	Urtica- ria	Hay- fever	Other allergy
Migraine material	39	8 %	21 %	23 %	5 %	8 %
Asthma material	40	—	60 %	25 %	0	18 %
Normal material	88	5 %	23 %	24 %	5 %	5 %

from the great difference in the incidence of allergic diseases in the normal persons themselves on the one hand (Table 2) and in their relatives on the other (Table 1).

Table 3 lists the factors that, according to the migraine patients themselves, provoked the attacks. It appears that allergy was suspected to be the inciting factor in only a very small number of cases, and that psychic factors dominated.

TABLE 3
Factors precipitating the attacks of migraine as elicited from the sick histories of the patients.

Number examined	Factors reported to bring on migraine				
	Allergy ¹⁾	Psychic factors ²⁾	Physical factors ³⁾	Menstruation ⁴⁾	Unknown
39	8 %	59 %	36 %	(29 %)	15 %

¹ Various foods.

² Tension, worry, late nights, etc.

³ Physical exertion, hunger, light, cold, etc.

⁴ 5 of 20 women over 15 years.

The allergen tests gave completely negative results in not less than 27 of 40 cases. However, 13 of the migraine patients tested showed positive skin reactions of varying strength to different allergens. The results are shown in Table 4. It appears from this table that the inhalation allergens dominated, while the nutrition allergens were only scantily represented with, oddly enough, not a single positive cutaneous reaction to vegetables. Three of the 13 patients with positive skin reactions had asthma, combined with *febris aestivalis* in one case and with urticaria and eczema in another. Two of the patients had eczema only and four gave a history of urticaria.

A comparison between the incidence and strength of the positive skin reactions in the present migraine material and the asthma material appears from Table 5. A distinct discrepancy will be noted.

TABLE 4
The types of allergies observed in 13 patients with migraine. A further 27 patients failed to give any positive intradermal reactions.

	Household dust	Mattress dust	Timothy pollen	Birch pollen	Cattle hair	Horse hair	Wool	Hazelnut	Lobster	Raw egg yolk	Boiled milk	Feathers	Allergic complaints
Case 4. K. A.	+++		++	++			++						Urticaria ¹
" 5. L. A.	++		++	++			++			+			—
" 9. I. C.	++		++	++			++		++	++		+	Eczema
" 13. M. H.	++	++	++	++	++	++	++	+					Urticaria
" 16. G. J.	++		++	++	++	++	++						Asthma, urticaria and eczema
" 18. S. J.	+		+	+	++	++	+						Urticaria
" 24. S. N.	++	++	++	+	++	++	++						Urticaria
" 26. G. P.	++	++	++	+	++	++	++		++				Urticaria
" 28. I. R.	++	++	++	++	++	++	++		++				Eczema
" 29. J. R.	++	++	++	++	++	++	++						— ²
" 33. T. S.	++	++	++	++	++	++	++	+		++	++	+	Asthma ³
" 34. A. T.	++	+	+	++	+	++	+	++					— ⁴
" 37. B. W.	++	+	+	++	++	++	++	++					Asthma and Febris aestivalis.

¹ Slightly positive reactions to hay and raw egg white also.

² Slightly positive reaction to uncooked milk only.

³ Slightly positive reactions to fish, straw, uncooked milk, and mould also.

⁴ Slightly positive reaction to barley also.

TABLE 5

The intensity of the skin reactions in a material of patients with migraine as compared with asthma patients.

Strength of intracutaneous reactions	Migraine material (40 cases)	Asthma material (40 cases)
+	21	47
++	18	75
+++		
++++	19	117
+++++		

As appears from Table 3, intake of certain foods was suspected as the cause of the migraine attacks in only three cases. Exposure experiments in the same three cases, the only ones to be made, were completely negative.

Treatment with *Antasten* tablets was tried in 14 cases. The preparation was given in doses corresponding to 4 to 5 mg. per kilogram body weight over a period of about one month. Seven cases suffered definite side-effects in the form of tiredness, nausea, and giddiness, which were severe enough in some instances to necessitate reduction of the dose. Two of the patients who had attacks of migraine on an average of two to four times a month reported a considerable improvement, which lasted for two or three months after cessation of the treatment. Four patients stated that there was some improvement during the course of the treatment, and the remaining eight observed no effect of the preparation whatever. In view of the well-known suggestibility of migraine patients, care must be taken not to overestimate the importance of occasional positive results. Similar results have previously been obtained by Kallós (1947).

DISCUSSION

The preceding results differ considerably from those observed by certain American allergologists. And even fewer positive findings were recorded than in the study of a Swedish

material recently published by Bergqvist (1948). What is the explanation?

Certain observations would suggest that the incidence of allergic diseases actually is greater in the United States than in Sweden. But this would scarcely account for a disproportionately high rate of allergic migraine. It is difficult to compare the total incidence of typical migraine in the two countries. A thorough analysis of the real incidence of migraine in Sweden has been conducted by Vahlquist et al. (1949). Certain investigations suggest that the mean incidence may be much the same in the United States (Balyeat and Rinkel, 1931, Grimes 1931).

In the present discussion, it is obviously of fundamental importance that the criteria for allergy be approximately uniform. We shall confine ourselves in this connection to the skin tests.

The extracts used in our tests (manufactured by the *Vitrum* company in Stockholm) presumably are not inferior to foreign products. They have been submitted to a series of thorough comparative clinical tests, and have yielded corresponding results in the hands of different investigators.

It is impossible to say how far differences in evaluation of the reactions obtained are to be blamed for discrepancies in the results. As appears from the description of the method, our reactions were always evaluated in relation to a standard histamine weal.

The number and the type of test extracts varies with different investigators. But even a comparison of the number of positive reactions with one and the same type of extract shows striking differences between the results obtained by American allergologists and those cited in the present study. The nutritional allergies predominate in the American reports, reaching as high as 100 per cent. In our series, on the other hand, the majority of positive reactions were due to inhalation allergies.

It cannot be denied that psychic factors play an important part in precipitating attacks of migraine. Proponents of the

allergic theory do not deny this, but claim that the psychic shock gives rise to a change in intestinal tone and peristalsis, which favours absorption of substances to which the patient is allergic. This line of reasoning seems to have little factual background. We have not been able to discover any roentgenological observations of stasis or antiperistalsis *before* an attack of migraine, whether spontaneous or provoked. That such changes may occur *during* the attack when the nausea has already developed is another matter; we have seen this happen ourselves in several cases.

Certain patients report that they regularly have attacks of migraine when they are under psychic strain, e.g. students after written examinations. It seems rather far-fetched to assume that the critical allergen or allergens are present in the intestine on all such occasions waiting to be absorbed just when absorption is going to be temporarily intensified.

Proof of the accuracy of the allergic theory in migraine is said to be found in the therapeutic results. Different allergologists report that between 50 and 80 per cent of patients treated by desensitization and/or elimination diet are cured or considerably improved (Eyermann, 1931; Balyeat, 1933; Hartsock and Mc Gurl 1938). These figures would be more convincing if other workers had not reported almost as good results with completely different treatments, which could not reasonably have had any effect on the allergic mechanisms. Grunert (1938), for example, stated that correction of refractive errors led to considerable improvement in 197 of 208 patients! Other workers report 60 to 70 per cent improved with histamine desensitization or with diet only (Goldzieher 1946). The endocrinologists have achieved excellent results with hormone treatment, and so on.

We do not doubt that in a certain number of cases, the attacks of migraine are really brought on invariably or on certain occasions by an allergic condition. But we believe that if good results are secured with an anti-allergic treatment in 60 to 80 per cent of a series, this is due in part to the cir-

cumstance that the material is a selected one from the point of view of allergy and in part to the well-known fact that migraine patients are suggestible, as well as susceptible to various measures which convince them that they have found an interested helper in their physician and that they must adhere to a specific regimen. Any kind of regimen is in itself an important form of psychotherapy to these individuals, who generally are very ambitious, but frequently inflexible and oppressed by a feeling of insecurity.

Our belief that the part played by allergy in precipitating attacks of migraine has been greatly over-estimated seems to correspond to that expressed by numerous well-known American physicians during the last few years. Wolff, for example, does not mention allergy or its treatment in "Management and prevention of migraine" in Cecil's Textbook (1947), and Palmer (1945) reported the elimination of allergy to be effective in at most 10 per cent of migraine cases.

As a conclusion to this paper, we should like to quote another prominent American physician, Dr. Alvarez of the Mayo Clinic (1947): "... the essential attribute of the typically migrainous person is his or her peculiar physical and mental and spiritual make up ... I always think of the migrainous storm in the brain as being like a mousetrap set off by a trigger. Allergy is just one of the things that can spring the trap."

SUMMARY

Forty persons with typical migraine were submitted to an allergy analysis. Skin tests gave positive results in 13 cases (Table 4 and 5). Seven of these showed multiple and in some cases strongly positive reactions; inhalation allergens were involved in the great majority of positive reactions. All seven patients had signs of allergic disease. The incidence of typical allergic diseases in the migraine patients themselves, as well as in their closest relatives, did not differ to any extent from

that in a control material (Tables 1 and 2). Treatment with a histamine antagonist (*Antasten*) had an appreciable effect in only 2 out of 14 cases.

The investigation does not support the theory that allergy is a common cause of migraine.

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