MIGRAINE IN CHILDHOOD *

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While migraine in later childhood differs in no respect from the disease as seen in the adult, its recognition in infancy and early childhood offers considerable difficulty, owing to the inability of the patient to describe symptoms accurately.

As is well known, migraine is often a hereditary disease, being directly inherited in about 50 per cent. of the cases. Not infrequently it has been known to occur in three or even four generations. It has not yet been ascertained whether or not the mendelian laws govern its inheritance. Like other hereditary diseases, it may be congenital, though this is exceptional. Such was the case with Russell's patient,¹ who had the first manifestations at the age of 2 weeks, with attacks regularly thereafter every two weeks; at the age of 7 years the disease changed to the ophthalmoplegic type.

Age at Onset.—In Flatau's² large series of 307 cases, the disease began most frequently from the sixteenth to the thirtieth year, but in 21 per cent. the onset was before this period and in 12 per cent. before the eleventh year. In only 1 per cent. did it begin during the first five years of life. Gowers,³ however, found a larger incidence in childhood, about one-third of his cases beginning between the fifth and tenth years, and two-fifths between the ages of 10 and 20. All writers agree that it is rare in the first half decade.

Symptomatology.—In infancy the symptoms are obscure and the attacks are of shorter duration than in the adult, lasting only a few hours. There are periodic attacks of vomiting, associated with pain and restlessness, and sometimes convulsions; the temperature is often somewhat raised. Constipation is the rule, in contrast with gastroenteritis, a disease which is in other respects somewhat similar to migraine at this period of life.

In early childhood the attacks are more like those in the adult, though the pain is less often localized in one side of the head, and sensory and ophthalmic symptoms are less common. Of great interest is the association with cyclic vomiting, which is apparently not very

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1. Russell, J. W.: Brit. Med. Jour., 1903, **1**, 1020.

2. Flatau, E.: Die Migräne, Berlin, 1912.

3. Gowers, W. R.: Diseases of the Nervous System, Ed. 2, 1898, **2**, 836.

uncommon. Usually cyclic vomiting appears first and is replaced later in childhood by migraine, but in the case of Comby⁴ migraine appeared at the age of 2, and was replaced by cyclic vomiting at the age of 8, while in one of Fabre's⁵ cases, a girl of 9, migraine came first, but did not cease with the appearance of cyclic vomiting.

The association with epilepsy is rare in childhood.

Increased intestinal putrefaction is a rather frequent accompaniment of migraine which is often overlooked. While it is not constant, and therefore cannot be the cause of the disease, it appears to aggravate the attacks, and hence is worthy of consideration. The examination of the urine for phenol will often reveal such putrefaction where the test for indican is negative. It cannot be too strongly emphasized that the amounts of phenol and of indican in the urine are quite independent of one another. The reason for this is that phenol is derived from the tyrosin portion of the protein molecule, while indican is derived from tryptophan. It is possible that one set of intestinal micro-organisms attacks tyrosin, and another tryptophan. A simple test for phenol in the urine is the following: 100 c.c. of urine are distilled with 5 c.c. of strong sulphuric acid until one-half of the liquid has gone over, and to the distillate is added bromin water in excess. The presence of a definite white precipitate (tribromphenol) indicates the presence of phenol in excessive amounts.

Recent work by Folin and Denis⁶ and by Dubin⁷ has thrown new light on the physiology of the phenols. This has been rendered possible by a new colorimetric method, devised by Folin and Denis,⁸ by which phenol, both free and combined, can be determined rapidly, and with accuracy. Contrary to the long-prevailing opinion, Folin and Denis have shown that the greater part (about 80 per cent.) of the phenol in the urine is normally excreted in the free state. Dubin, however, found that if phenol is administered in large amounts to dogs, a very marked increase in the conjugation takes place. It would appear, therefore, that the protective mechanism by which phenol is rendered harmless is called into play only when excessive amounts have to be cared for. The total amount of phenol, both in animals and in man, was found to vary directly but not proportionally with the intake of protein. After the use of enemas and of cathartics the amount is lowered appreciably.

The nature of migraine is still little understood. The analogy with epilepsy is very close; in both conditions there is a strong heredi-

4. Comby, J.: *Arch. de méd. d. enf.*, 1901, **4**, 9, Observation 11.

5. Fabre, E.: *Migraine chez les enfants*. Thèse de Paris, 1904.

6. Folin, O., and Denis, W.: *Jour. Biol. Chem.*, 1916, **26**, 507.

7. Dubin, H.: *Jour. Biol. Chem.*, 1916, **26**, 69.

8. Folin, O., and Denis, W.: *Jour. Biol. Chem.*, 1915, **22**, 309.

tary element; in both periodic cerebral attacks, affecting in the one case the sensory, in the other the motor sphere. Moreover, the two diseases often have been found in the same person, migraine occurring first, being replaced later by epilepsy.

A comparison with asthma, another hereditary disease, suggests another point of view. Here again are periodic attacks, with intervals of good health. The symptoms of asthma resemble closely those of anaphylactic shock in the guinea-pig, and for many cases a hypersusceptibility to certain proteins has been demonstrated. It has been attempted to explain migraine also as a manifestation of anaphylaxis, but thus far without success. It is true that indiscretions in diet may precipitate an attack of migraine, and that a low protein diet is beneficial in some, though by no means in all cases, but hypersusceptibility to proteins has not been shown by direct methods, eosinophilia has not been reported, and the symptoms are not similar to those of experimental anaphylaxis.

A disorder of metabolism is another possibility, for which there are analogies among inherited diseases, such as diabetes and gout, in which there is direct heredity, and those rare anomalies of metabolism, pentosuria, cystinuria and alkaptonuria, in which, however, the condition is congenital and familial but not hereditary. Moreover, diseases of metabolism may show marked periodicity, as in gout, and that rare disease known as family periodic paralysis, in which Edsall and Means⁹ have recently shown decided disturbances of metabolism, in the shape of increased basal metabolism during attacks, and a long continued marked increase of the nonprotein nitrogen of the blood, in the absence of nephritis. Very little work has been done on the metabolism in migraine, and this should offer a good field for future investigation.

It often has been attempted to explain the symptoms of migraine on the basis of an abnormal reaction of a diseased central nervous system to stimuli which in the healthy person would produce no effect. In favor of this view various signs of a disturbed vasomotor and sympathetic innervation during the attack have been adduced. But this theory altogether fails to explain the most striking feature of migraine, namely, the periodicity of the attacks, and the sense of well being during the intervals.

To sum up, the cause of migraine remains obscure. The hypothesis of intoxication by the products of a disordered metabolism seems at present to offer the best basis for investigation.

Diagnosis.—The diagnosis rests chiefly on the periodic occurrence of headache, accompanied usually by nausea and vomiting. The

9. Edsall, D. L., and Means, J. H.: Am. Jour. Med. Sc., 1915, **150**, 169.

intervals between attacks vary from one to two weeks up to several months in duration, and are free from symptoms, unless the attacks follow one another very closely. It is not essential that the headache should be confined to one side; in case it is not, it is usually frontal, rarely occipital. Scintillating scotomas, numbness of one side of the body and other ophthalmic and sensory symptoms are not a necessary part of the disease, and in fact are rare in childhood. A family history of migraine is of much diagnostic value. In young children the diagnosis may be difficult on account of their inability to describe symptoms. The periodicity of the attacks, however, and the state of well-being between them, together with the exclusion by careful physical examination, of other causes of headache, will usually enable one to arrive at the correct conclusion.

From cyclic vomiting it is differentiated by the following features: in migraine the headache precedes the vomiting, and is the predominating symptom, while in cyclic vomiting the headache is usually not severe, and the vomiting is frequent and intractable. The presence of large amounts of acetone in the urine is constant in cyclic vomiting, and also in migraine providing vomiting is present, but in the former it may precede the attack, and in that case has diagnostic value.

Treatment.—A thorough examination of the patient, with especial attention to the eyes, nose, throat, accessory sinuses, teeth and digestive tract, is a prerequisite of intelligent treatment. While it is doubtful if true migraine has ever been cured by the correction of refractive errors, of nasal troubles or by alterations of the diet, it is true that any measure that improves the patient's general condition is likely to ameliorate the severity of the attacks, and to reduce their frequency. For this reason any abnormalities which are capable of correction should receive attention.

The diet is of considerable importance. It is well known that some persons have fewer attacks if meat and fish are excluded. This effect was formerly attributed to the influence of a purin-poor diet on the uric acid diathesis, which was erroneously supposed to play an important part in migraine. It may well be due to the reduction of an increased intestinal putrefaction, a factor which should always be looked for. If it is present, meat, fish and eggs should be excluded from the diet, and the effect on the excretion of phenol and indican noted. In some cases it may be even necessary to exclude milk to attain the desired result. Constipation, if present, of course should be corrected, as tending to increase intestinal putrefaction.

In a few cases attacks apparently are precipitated by overindulgence in carbohydrates, such as candy.

Attention to hygiene is an essential part of the treatment. It is often necessary to withdraw the child from school for a while, and to limit

the hours of study and reading. An abundance of fresh air and exercise in amounts suited to the individual are indicated.

The use of drugs during the attack should be limited, since in small doses they have no effect, and in large doses they are apt to be deleterious. Of the antineuralgics, caffeine seems to have the best effect. Morphin may be required in very severe paroxysms. The administration of drugs during the intervals, with the purpose of reducing the severity and frequency of attacks, has proved disappointing in my hands, though recommended by Oppenheim and other authorities.

By the use of the above measures the frequency and severity of the attacks are usually lessened, but it is doubtful if true migraine is ever cured.

The following case seems worthy of report on account of the unusually early incidence of the disease and the presence of large amounts of phenol in the urine.

REPORT OF CASE

History.—H. B., a boy, aged 6 years, was seen March 1, 1918, in consultation with Dr. H. M. Steele.

Family History.—The maternal grandmother and a maternal aunt have suffered severely from typical migraine. The parents and a sister aged 4 years are free from headache.

Past History.—This is negative except for the fact that as an infant he used to lick the paint off the bed.

Present Illness.—Since the age of 3 years, he has been subject to periodic attacks of headache, accompanied by vomiting. Acetone occurs abundantly in the urine at these times, a feature which had led to the diagnosis of cyclic vomiting. The attacks come at intervals of from one to three months, as a rule, but during the previous winter have occurred about once a week. There is an aura the day before, consisting of pallor, nervousness and an abnormal appetite, usually poor, but sometimes increased to a pathologic degree. The headache is intense and always precedes the vomiting; it is bilateral and frontal in distribution and accompanied by photophobia. The duration of the attack is about twenty-four hours. Between attacks the boy is well and free from headache. There has been a distinct intolerance of eggs; if he takes more than one egg a week he is almost certain to have an attack. He has not taken large quantities of meat.

Physical Examination.—A fairly developed boy, 45 inches in height, weighing only 37 pounds (the normal weight for this age is 45 pounds). The head is rather square, but there are no other signs of rickets. The tonsils are moderately enlarged. The heart, lungs, abdomen and reflexes are negative. The systolic blood pressure measures 82 mm., the diastolic 50. The examination of the eyes by Dr. E. M. Blake, shows a considerable degree of hypermetropia (+2 D.). The hemoglobin is 90 per cent. The blood smear shows a considerable increase in lymphocytes, the count being as follows: polynuclear nuclears, 35 per cent.; lymphocytes, 58.5 per cent.; large mononuclear and transitional cells, 4 per cent.; eosinophils, 1 per cent., and mast cells, 1.5 per cent. The red cells are normal.

Urine: Twenty-four hour amount, 500 c.c., color normal, reaction acid, specific gravity 1.015, albumin sugar and indican absent, *phenol present in large amounts*, acetone present (during the attack), sediment negative. Examination of the feces for lead is negative.

Treatment.—The treatment consisted in withdrawal from school, the correction of the refractive error and alteration of the diet. Throughout the month of March no meat or fish was eaten. During April the child was put back on his former diet. It was now found that he had an increased tolerance for eggs, which he craves, being able to take three or four a week without headache. Examination of the urine April 16 and May 22 still showed large amounts of phenol; during March, when the protein intake was restricted, no examination was made. In spite of the phenoluria he has been practically free from headache since beginning of treatment, having had but one slight attack from March to the date of writing, June, 1918.

COMMENT

The beneficial effect of even a temporary diminution of the protein intake is shown in the almost complete disappearance of the headaches, and in the increased tolerance of eggs. Further restriction of protein is indicated, until the excretion of phenol reaches normal limits.

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